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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,096	09/18/2003	Brian R. MacDonald	PRD-2110-USANP	1638

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/667,096	MACDONALD ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 September 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/26/04; 3/26/04; 5/22/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 22 May 2006 has been entered in full. Claims 3 and 7-12 are amended. Claim 1 is cancelled. Claims 13-30 are added.

Election/Restrictions

Applicant's election without traverse of Group II, claims 2-12, drawn to methods comprising the steps of administering a TPO mimetic compound to a subject in the reply filed on 22 May 2006 is acknowledged.

Applicant's election with traverse of the species of TPO mimetic (I E G P T L R Q (2-Nal) L A A R X_{10}, where X_{10} is sarcosine or β-alanine in the reply filed on 22 May 2006 is acknowledged. The traversal is on the ground(s) that a search and examination for the compounds disclosed in the present application will not place an undue search burden on the Office. This is found persuasive because the species of TPO mimetics shown in Figure 2 of the instant application are already well known in the prior art (see for example, Dower et al. U.S. Patent 5,869,451). Thus, the species election requirement between TPO mimetics is *withdrawn*.

Claims 2-30 are under consideration in the instant application.

Information Disclosure Statement

It is noted that reference WO 01/21180, cited on the information disclosure statement of 22 May 2006, has been crossed off by the Examiner because it was cited in duplicate (see IDS submitted 26 March 2004).

Drawings

1. Figure 2 should be designated by a legend such as --Prior Art-- because only that which is old is illustrated. See MPEP § 608.02(g). Corrected drawings in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

2. The disclosure is objected to because of the following informalities:

3. The Brief Description of the Drawings at pg 5 of the specification and the amendment of 27 February 2006 describe the wrong figures. For instance, the description of Figure 1 in the specification actually describes the drawing labeled Figure 2 (a list of compounds). The original description of Figure 2 in the specification describes the bloodstream diagram that is shown in the drawing labeled Figure 1. It is also noted that pages 6 and 8 make references to the incorrect Figures. (Please note that this issue could be overcome by resubmitting new Figures that have been relabeled or by amending the specification.)

4. The specification contains a blank at pg 6, line 12, which is not clear, concise, and exact. Appropriate correction is required.

Claim Objections

5. Claims 2, 7-15, 20, 21, and 26 are objected to because of the following informalities:

5a. Regarding claims 2, 7-15, 20, 21, and 26, the acronym "TPO" should be spelled out in all independent claims for clarity.

5b. Regarding claim 8, the acronym "PK" should be spelled out in all independent claims for clarity.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 2-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 2-30 are indefinite because the elements recited in the claim do not constitute proper Markush groups. The claims are indefinite in the alternative use of "and/or" because it is not clear what controls which of these limitations. See MPEP § 2173.05(h).

8. Claims 2-30 are indefinite because it cannot be determined if the harvested stem cells are transplanted into a different subject (i.e, a recipient) or if they are administered to the same subject from which they were taken. If the cells are administered to the same subject from which they were taken, then there seems to be a step missing between harvesting and transplanting the cells. For example, after harvesting the cells, does the patient undergo chemotherapy or other bone marrow ablative treatments?

9. Claims 2-30 recite the limitation "one or more of the bone marrow stem cells" (see claim 2, line 5, for example). There is insufficient antecedent basis for this limitation in the claim. It is not clear if this limitation is intended to refer to one or more stem cell *populations* (see claim 2, lines 3-4, for example).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 2-6 and 9-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Fibbe et al. (U.S. Patent 6,013,067; January 11, 2000).

Fibbe et al. teach a method for increasing platelets or erythrocytes and a method for stimulating platelet or erythrocyte recovery in a patient comprising (1) administering to a donor an amount of TPO sufficient to stimulate proliferation of cells of the myeloid lineage, (2) collecting bone marrow cells or peripheral blood stem cells from the donor, and (3) administering the bone marrow cells or peripheral blood stem cells to a recipient patient (col 1, lines 55-63; claims 1, 13, for example). Fibbe et al. disclose that cells of the myeloid lineage include CD34+ stem cells and cells derived from CD34+ stem cells (col 4, lines 1-7). Fibbe et al. teach that the donor and recipient may be different individuals or the same individual (col 1, lines 63-64). Fibbe et al. also teach that bone marrow cells may be collected from the patient prior to chemotherapy or radiation therapy and returned to the patient subsequent to the therapy (col 2, lines 16-21). Fibbe et al. teach that collected marrow cells are cryopreserved according to

established procedures and thawed prior to use (col 3, lines 60-65). Fibbe et al. teach that the use of allelic and engineered variant TPOs is contemplated, as well as truncated forms of TPO (col 3, lines 8-20).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

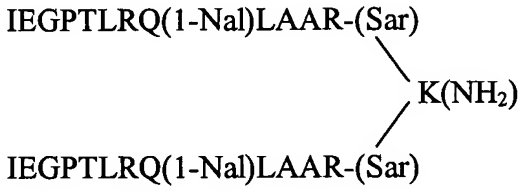
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 7-8 and 13-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fibbe et al. (U.S. Patent 6,013,067) as applied to claims 2-6 and 9-12 above, and further in view of Dower et al. (U.S. Patent 5,869,451).

The teachings of Fibbe et al. are set forth above.

Fibbe et al. does not teach that the TPO mimetic compound utilized in the method has reduced immunogenicity relative to one or more of rhTPO and rhIL-11 or that the compound has an improved PK profile relative to one or more of rhTPO and rhIL-11. Fibbe et al. does not teach any specific TPO mimetic sequence other than TPO. Fibbe et al. does not teach that the TPO mimetic compound is covalently attached to a hydrophilic polymer.

Dower et al. teach TPO mimetic compounds that have strong binding properties to the TPO receptor and that can activate the TPO receptor. For example, Dower et al. disclose TPO mimetic compounds with the following sequences : IEGPTLRQWLAAR-Sar (SEQ ID NO: 215) and IEGPTLRQ(1-Nal)LAAR-Sar (SEQ ID NO: 216) (col 5, 57-58; claim 1). Dower et al. teach that a preferred synthetic amino acids include L-(2-naphthyl)-alanine (1-Nal) and L-(2-naphthyl)-alanine (2-Nal). Dower et al. disclose that peptide compounds may be dimerized or oligermized to increase the affinity and/or activity and disclose a TPO mimetic compound with the formula (col 5, 57-58; claim 1):



Dower et al. teach that the TPO peptides may be covalently attached to one or more hydrophilic polymers, including polyethylene glycol (bottom of col 5 through top of col 6; col 33, lines 4-25). Dower et al. discloses that when peptide compounds are derivatized with a hydrophilic polymer, their solubility and circulation half-lives are increases and their immunogenicity is masked (col 32, lines 39-46). Dower et al. continues to teach that hydrophilic

polymers have an average molecular weight ranging from about 500 to about 100,000 daltons, more preferably from about 2,000 to about 40,000 daltons, even more preferably from about 5,000 to about 20,000 daltons (col 32, lines 55-62). Dower et al. also teach that several PEGylated TPO peptides have an increased pharmacokinetic profile (col 59-62).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method for increasing platelets or erythrocytes and the method for stimulating platelet or erythrocyte recovery in a patient as taught by Fibbe et al. by utilizing the TPO mimetic compounds as taught by Dower et al. The person of ordinary skill in the art would have been motivated to make that modification because peptide mimetics have advantages over polypeptides, such as more economical production, greater chemical stability, altered specificity, enhanced pharmacological properties, and reduced antigenicity (see Dower et al.; col 14, lines 13-19). The person of ordinary skill in the art reasonably would have expected success because peptide mimetics of other receptor-binding peptides were already being generated and utilized in methods at the time the invention was made. Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

Conclusion

No claims are allowable.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Liu et al. U.S. Patent 6,835,809 (small TPO peptide compounds)

WO 98/25965 (TPO peptide mimetics)

Cwirla et al. Science 276 : 1696-1699, 1997 (small TPO peptide agonists)

Fibbe et al. Blood 86(9) : 3308-3313, 1995 (pretreatment of donor animals with TPO before marrow procurement accelerates the reconstitution of platelets and erythrocytes after stem cell transplantation)

Dower et al. Stem Cells 16(Suppl 2) : 21-29, 1998 (TPO peptide agonists)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
24 July 2006

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER